Concomitant aortic valve replacement and coronary bypass: the effect of valve type on the blood flow in bypass grafts

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Abstract

Objective: In cases of aortic valve replacement, the downstream flow profile and turbulence in the ascending aorta differ according to the prosthetic aortic valve implanted. The objective of this work is to study the influence of prosthetic valve type on the flow in the bypass grafts implanted to the ascending aorta in cases of concomitant aortic valve replacement and coronary artery bypass. Methods: The study is conducted on 456 patients receiving concomitant aortic valve replacement and coronary bypass vein grafts anastomosed to the ascending aorta. The patients included in the study received a total number of 725 vein grafts, 249 biological aortic valves and 207 mechanical aortic valves. Intraoperative transit time flow measurement was done for all bypass grafts and a multiple regression model was calculated for the factors influencing the flow in the bypass grafts. Results: The mean flow in vein grafts in patients receiving biological valves was 49.79 ± 26.88 ml/min, while in patients receiving mechanical valves it was 46.54 ± 26.68 ml/min. The multiple regression model revealed that receiving a mechanical valve is an independent risk factor for lower flow in the vein grafts. Conclusions: The type of the aortic valve implanted and consequently the downstream flow profile in the ascending aorta do affect the flow in the vein grafts in cases of concomitant aortic valve replacement and coronary bypass. Receiving a mechanical aortic valve is an independent risk factor for lower flow in the vein grafts.

Keywords: Aortic valve replacement; CABG; Hemodynamics

1. Introduction

In normal aortic valves the velocity profiles in the ascending aorta are generally flat during the acceleration phase. At peak systole a skew develops, with the highest velocities closer to the posterior, right, and finally anterior aortic wall [1].

Turbulent flow is characterized by an unsteady and irregular eddying motion that is superimposed on the mean flow [2]. Studies both in vitro [3,4] and in animals [2,5,6] have demonstrated turbulent blood flow downstream of different types of prosthetic valves. The effect of turbulent flow in the ascending aorta after aortic valve replacement on native coronary blood flow was studied in animal models [7]. The study found significant decrease in coronary blood flow with increasing blood turbulence by rotating the mechanical valves away from the optimal orientation. The choice of the aortic valve prosthesis was also found to affect the blood flow in the native coronary arteries in human patients [8,9].

To our knowledge, the effect of the prosthetic valve type on blood flow in coronary bypass grafts anastomosed to the ascending aorta has not been studied, neither in animal models nor in patients. The objective of this work is to study such effect in patients receiving concomitant aortic valve replacement and coronary artery bypass.

To study the blood flow in bypass grafts, transit time flow measurement (TTFM) was used. TTFM has recently been introduced as an effective and reliable method for intraoperative evaluation of blood flow in coronary bypass grafts [10,11].

2. Patients and methods

Between January 1998 and December 2005, 456 patients underwent concomitant aortic valve replacement with coronary artery bypass using vein grafts anastomosed to the ascending aorta, and all of them were included in the study. Patients with replacement of the ascending aorta or aortic root were not included.

The choice of the valve whether mechanical or biological was decided after thorough discussion with the patient.

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explaining the advantages and disadvantages of each type and addressing the specific patient’s factors favoring one type over the other, e.g., age, need for anticoagulation for other reasons, renal insufficiency, contraindication for anticoagulation. All patients have signed an informed consent for the operation and for quality control measures including flow measurements, and received a copy of flow measurements after discharge. All laboratory, anesthesiological and surgical data, as well as data derived from complete postoperative 30 days follow up were retrieved from the consolidated database of our Data Mart system.

2.1. Operative procedures

Cardiopulmonary bypass was performed with standard equipments and techniques under systemic normothermia and cardiac arrest achieved using both antegrade and retrograde cold hyperkalemic blood. Distal coronary anastomoses were performed first using 7-0 continuous prolene followed by valve implantation and lastly proximal anastomoses using 6-0 continuous prolene. The site of the proximal anastomosis was chosen so that the bypass graft takes an optimal course without kink or tension. The aortic cross clamp was removed after finishing the proximal anastomoses.

Mechanical valves and stented biological valves were implanted using pledgeted mattress sutures of 2-0 Ethibond. Stentless valves were implanted using the subcoronary technique with 4-0 continuous prolene in both proximal and distal suture lines.

During the implantation of the mechanical valves, care was taken to implant them in the optimal orientation, with the major orifice of the monoleaflet valves facing the noncoronary sinus and one of the orifices of the bileaflet valves facing the right coronary sinus and the other orifice facing the left coronary sinus.

Intraoperative transesophageal echocardiography was done for all patients to exclude any valve malfunctioning or perivalvular leak.

2.2. Transit time flow measurement

Transit time flow was measured in all bypass grafts before reversal of heparin. The same device was used for measurement in all cases; Transonic Flow Measurement HT311 (Transonic Systems Inc., Ithaca, NY 14850 USA) with probes measuring between 2 and 4 mm in size to fit perfectly around the graft.

Before making any measurement, adequate systemic blood pressure was maintained. In patients with borderline values, flow measurement was repeated once or twice including at least one time just before sternal closure and the best value was recorded. The mean flow in milliliters per minute and the pulsatile index were recorded. The PI, expressed as an absolute number, is considered a good indicator of the quality of the anastomosis [11].

2.3. Statistical analysis

The Mean flows were expressed as mean ± SD. To study the effect of aortic valve prosthetic type on the blood flow in the bypass grafts while controlling for the many possible confounders multiple regression models for the mean flow in bypass grafts were calculated. Initially 22 variables were studied (Appendix A). To obtain the final multiple regression model, the variables with a difference in the outcome variable (mean flow) with a $P$ value smaller than or equal to 0.25 were included in multiple regression models in a stepwise way till no further decrease in the Akaike Information Criterion was observed (AIC = deviance of the model + 2 x number of included parameters). In order to search for the optimal relation with the mean flow, continuous variables were transformed (square, square root, log, exp, reciprocal and into nominal categories) and combinations of risk factors were also included if the AIC could be further decreased. All statistics were obtained by the Version 5 of the JMP® Software (SAS Institute Inc.).

3. Results

The study was performed on 456 patients with concomitant aortic valve replacement and coronary artery bypass using vein grafts anastomosed to the ascending aorta. Of these patients 249 (54.6%) received biological valves (142 stented and 107 stentless) and 207 (45.4%) mechanical valves (138 bileaflet and 69 monoleaflet). The indication of aortic valve replacement was aortic stenosis in 228 patients (123 received biological and 105 received mechanical valves), aortic incompetence in 26 patients (7 received biological valves and 19 mechanical valves) and combined aortic stenosis and incompetence in 202 patients (119 received biological and 83 received mechanical valves).

The bileaflet mechanical valves used were 129 St Jude Medical (SJM) (St Jude Medical, Inc, St Paul, MN), 5 Carbo-Medics (CM) (Carbo-Medics, Austin, TX), and 4 Medtronic Advantage (Medtronic, Minneapolis, MN). All monoleaflet mechanical valves were Medtronic Hall (MH) (Medtronic, Minneapolis, MN). The stented biological valves were 108 Medtronic Mosaic (Medtronic, Minneapolis, MN) and 34 Carpentier-Edwards Perimount (Baxter Healthcare Corp., Irvine, CA). All stentless valves were Medtronic Freestyle (Medtronic, Minneapolis, MN).

There were 205 left internal mammary to LAD grafts, 101 of which to patients receiving biological valves (0.4 graft/patient) and 104 to patients receiving mechanical valves (0.5 grafts/patient). The vein grafts were 725, of which there were 393 to patients receiving biological valves (1.6 vein grafts/patient) and 332 to patients receiving mechanical valves (1.6 vein grafts/patient).

The mean age of patients receiving biological valves was 76 ± 5.7 years, while the mean age in patients receiving mechanical valves was 66.6 ± 7.7 years ($P < 0.01$). Among the patients receiving biological valves there were 107 females (43%) versus 53 females (25.6%) in patients receiving mechanical valves ($P < 0.01$). The mean body mass index of the mechanical valves group was 27.28 ± 4.21 and of the biological valves group was 26.46 ± 4.03 ($P < 0.01$). The mean Euro-SCORE for the patients receiving biological valves was 8.2 ± 2.2, while in patients receiving mechanical valves it was 6.4 ± 2.7 ($P < 0.01$).

Despite of less body mass index and more female patients, the flow in vein grafts in patients with biological valves was
higher than in the mechanical valve group (Table 1). Because both groups are significantly different in factors likely to influence the flow in bypass grafts, a multiple regression model was done. Initially, 22 variables were studied (Appendix A) and the final model was obtained as previously described.

Receiving a mechanical valve was found to be an independent risk factor for low flow in the bypass grafts ($P = 0.027$). For an alpha value for 0.05, the power was 0.603 and the adjusted power 0.508. The least significant number is 566 grafts and the least significant value is 1.91 ml/min. The 95% confidence interval of the difference in the vein graft mean flow between biological and mechanical valve was 0.21—7.81 ml/min.

Table 2 shows the factors influencing the flow in bypass grafts according to the multiple regression model. The multiple regression model was then recalculated after subdividing each of biological and mechanical valves into two subgroups as done in the analysis of the flow in vein grafts, no subgroup was found influencing the flow in the mammary graft. Female sex (estimate = –7), PI (estimate = –5.053) and aortic clamp time (estimate = –0.248) were found to be the independent factors influencing the flow in the mammary graft with $P = 0.037$, $P < 0.01$ and $P < 0.01$, respectively.

Postoperatively, there were 11 mortalities and 2 myocardial infarctions in patients receiving biological valves (4.4 and 0.8%, respectively) versus 5 mortalities and 2 myocardial infarctions in patients receiving mechanical valves (2.4 and 0.97, respectively). The differences were not statistically significant ($P = 0.311$ and $P = 1$, respectively).

### Table 1

<table>
<thead>
<tr>
<th>Term</th>
<th>Mean (ml/min)</th>
<th>SD</th>
<th>25% Quartile</th>
<th>Median</th>
<th>75% Quartile</th>
<th>SD</th>
<th>25% Quartile</th>
<th>Median</th>
<th>75% Quartile</th>
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<tr>
<td>Biological valve</td>
<td>46.54</td>
<td>4.32</td>
<td>27.59</td>
<td>41.38</td>
<td>58.31</td>
<td>5.52</td>
<td>27.16</td>
<td>41.11</td>
<td>45.84</td>
</tr>
<tr>
<td>Graft to diagonal</td>
<td>–2.667</td>
<td>1.421</td>
<td>–1.88</td>
<td>–2.71</td>
<td>0.415</td>
<td>0.234</td>
<td>–1.88</td>
<td>–1.88</td>
<td>–1.88</td>
</tr>
<tr>
<td>Pulsatility index</td>
<td>–8.858</td>
<td>0.105</td>
<td>–8.72</td>
<td>–8.72</td>
<td>–0.226</td>
<td>0.056</td>
<td>–8.72</td>
<td>–8.72</td>
<td>–8.72</td>
</tr>
<tr>
<td>Female</td>
<td>–5.672</td>
<td>2.499</td>
<td>–2.27</td>
<td>–2.27</td>
<td>0.079</td>
<td>0.04</td>
<td>–2.27</td>
<td>–2.27</td>
<td>–2.27</td>
</tr>
<tr>
<td>Body mass index</td>
<td>0.415</td>
<td>0.234</td>
<td>1.77</td>
<td>1.77</td>
<td>0.079</td>
<td>0.04</td>
<td>1.77</td>
<td>1.77</td>
<td>1.77</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>–0.226</td>
<td>0.056</td>
<td>–4</td>
<td>–4</td>
<td>0.079</td>
<td>0.04</td>
<td>–4</td>
<td>–4</td>
<td>–4</td>
</tr>
<tr>
<td>Cross clamp time</td>
<td>0.079</td>
<td>0.04</td>
<td>1.94</td>
<td>1.94</td>
<td>0.079</td>
<td>0.04</td>
<td>1.94</td>
<td>1.94</td>
<td>1.94</td>
</tr>
<tr>
<td>Intercept</td>
<td>79.203</td>
<td>14.942</td>
<td>5.3</td>
<td>&lt;0.01</td>
<td>79.203</td>
<td>14.942</td>
<td>5.3</td>
<td>&lt;0.01</td>
<td>5.3</td>
</tr>
</tbody>
</table>

**Term Estimate SE t Ratio P > |t|**

- Biological valve: 2.157 0.97 2.22 0.027
- Graft: –2.667 1.421 –1.88 0.061
- Pulsatility index: –8.858 0.105 –8.72 <0.01
- Female: –5.672 2.499 –2.27 0.024
- Body mass index: 0.415 0.234 1.77 0.077
- Ejection fraction: –0.226 0.056 –4 <0.01
- Cross clamp time: 0.079 0.04 1.94 0.053
- Intercept: 79.203 14.942 5.3 <0.01

The multiple regression analysis revealed no influence of valve type on the flow in the mammary graft ($P = 0.555$). With subdividing each of biological and mechanical valves into two subgroups as done in the analysis of the flow in vein grafts, no subgroup was found influencing the flow in the mammary graft. Female sex (estimate = –7), PI (estimate = –5.053) and aortic clamp time (estimate = –0.248) were found to be the independent factors influencing the flow in the mammary graft with $P = 0.037$, $P < 0.01$ and $P < 0.01$, respectively.

### 4. Discussion

Concomitant aortic valve replacement and coronary artery bypass is a common operation in most cardiac centers. Since coronary artery bypass grafting commonly includes one or more vein grafts as aorta-coronary bypass, the flow profile and turbulence downstream the prosthetic aortic valve should always be considered in these cases. This is especially important in grafts with border-line flow and in patients receiving multiple grafts.

The absence of laminar blood flow is well known to cause activation of blood platelets and coagulation cascade, so that turbulent flow patterns contribute to thrombus formation. [12,13] Turbulent flow has also an adverse effect on hemodynamics leading to increased myocardial stress, [14] a state that is less tolerated in patients with coronary artery disease.

Despite these studies, the effect of the turbulence downstream prosthetic aortic valves on vein grafts anastomosed to the ascending aorta has not been adequately studied. Our study demonstrates that the downstream flow profile does affect the flow in the bypass grafts. Receiving a mechanical aortic valve was found to be an independent risk factor for low flow in the bypass grafts. It might be argued that a difference of 3.25 ml/min is not clinically significant. Nevertheless, it is important to remember that this difference occurred despite the presence of factors having negative influence on the bypass blood flow in the biological valves group (significantly lower body mass index and more females with estimate impact on flow of –0.42 and –5.67
subsequently (Table 2). If both groups were similar, the difference in flow would have reached 9.34 mL/min/graft (20.1% difference), which can be clinically significant.

By further subdividing mechanical valves into monoleaflet and bileaflet valves, we found that receiving a monoleaflet aortic valve is an independent risk factor for low flow in vein grafts. Nevertheless, six studies found that monoleaflet mechanical valves in their optimal orientation demonstrate a superior hemodynamic performance [2,7,15–18].

The axis of the left ventricle, ascending aorta and aortic arch describe a curved course with different segments of the curve having different radii. In addition, the left ventricle has a spiral ejection pattern. [2] Thus, the flow pattern at the level of the aortic valve is asymmetric, showing highest flow along the noncoronary leaflet with a counterclockwise rotation of 90° between commissures [1]. It is obvious that the large opening of the asymmetrically constructed valves must be positioned to pass the larger part of the systolic stroke volume. This was confirmed in the above mentioned studies [2,7,15–18], which showed that the flow downstream the monoleaflet valves is very sensitive to rotation with the best profiles achieved when the large orifice faces the noncoronary sinus.

However, little attention was given in these studies to the turbulence in the ascending aorta away from the zone of high flow. Vein grafts are mostly implanted in the ascending aorta to the left of the high flow zone and accordingly, the flow in these grafts is likely to be affected by turbulence in the low flow zone of the ascending aorta, even if the flow profile in the high flow zone was nearly physiologic. In addition, four of these studies [2,7,17,18] were performed on animal models using a special rotation device to allow accurate orientation of the valve after closure of the aorta. These animal models had a normal native aortic valve and non-remodeled left ventricle. These circumstances are clearly different from what is seen in practice. A study performed on patients [15] evaluated the hemodynamic performance by measuring HITS using transcranial Doppler. However, a definite correlation of HITS with the hemodynamic [17] and clinical [19] findings could not be proved. The other study conducted on patients [16] demonstrated a three-dimensional computer construction of the flow profile in the ascending aorta using perivascular Doppler. Unfortunately, the methods and the results are very briefly described. It is also important to mention that there are common authors in all six studies and five of these studies [2,15–18] were conducted in one center.

By further subdividing biological valves into stented and stentless valves, we found that receiving a stented biological aortic valve is an independent factor for high flow in vein grafts. Stentless aortic bioprosthesis are well known to be associated with excellent hemodynamics [20,21]. Nevertheless, in cases of subcoronary implantation technique used in the patients included in our study; these superior hemodynamics could be demonstrated only after few months of implantation [22]. This improvement of hemodynamics can be explained by the resolving paraprosthetic edema and hematoma [23].

The results of our study raise an obvious question. Does the flow downstream the aortic prostheses influence the flow in the native coronary arteries as it does in bypass grafts? This assumption was demonstrated in animal models [7] as well as in human patients [8,9]. The two studies performed on patients revealed better blood flow in the native coronary arteries after stentless aortic valve implantation in comparison with stented valves. However, the few number of patients included in these studies is an important limitation of their results. The first study [8] randomized 24 patients to receive either a stented or a stentless bioprosthesis, while the second study [9] randomized 20 patients to receive either a stented or a stentless bioprosthesis and other 20 patients to receive either a monoleaflet or a bileaflet mechanical valve. It has been shown that the turbulence downstream the aortic prosthesis is best demonstrated 4 cm distal to the aortic valve [6,16]. Since this is the level where vein grafts are commonly anastomosed to the aorta, and considering the histological changes that occur in their wall after implantation [24], the blood flow downstream the aortic prosthesis is clearly more relevant for vein grafts than for native coronary artery.

In order to evaluate the bypass grafts, several technologies are now available. Coronary angiography is considered the gold standard for assessment of bypass grafts. However, it is costly, invasive, time consuming and utilizing ionizing radiation. Although it is possible to perform coronary angiography intraoperatively, it has never gained popularity for routine use because of the above mentioned limitations. Another imaging technique is thermal coronary angiography. This technique uses an infrared camera to detect temperature differences between graft injectant and the adjacent myocardium resulting in a ‘heat picture’. Although it is non invasive, it did not get enough popularity because it requires a relatively expensive thermal camera, and the anastomotic sites are not routinely clearly seen [25]. The most recent imaging technology for graft evaluation is the fluorescence imaging utilizing indocyanine Green exposed to near infrared light [26]. Like other imaging techniques, its use is very limited. The imaging technique that seems to be the most promising is the high frequency epicardial echocardiography. However, it is still evolving and its high cost is limiting its spread.

As none of imaging techniques is now applicable for routine use, non-imaging techniques have been developing. Electromagnetic waves were frequently used to measure the flow in bypass grafts [27]. This method measures the deflection of magnetic force created by the movement of iron atoms in the hemoglobin complex, and therefore such measurements depend on the concentration of serum hemoglobin. In addition, minor changes in the angle between the probe and the vessel affect the accuracy of the measurement.

Recently, electromagnetic flowmeters have been replaced by ultrasound technology. Nowadays transit-time flow probes, like those used in this study, are the most commonly used devices for assessment of flow in bypass grafts, as they are easy to use intraoperatively and they have proven high reliability and accuracy. A correlation has been found between the intraoperative flow and short-term graft occlusion [10]. Furthermore, low flow in grafts to LAD measured by TTFM was found to be associated with higher incidence of postoperative angina [28]. However, many factors are likely to affect TTFM. Accordingly, calculating a multiple regression model was essential to achieve reliable results. Also using the internal mammary artery grafts as...
control group was equally important. Our study could demonstrate that the type of the aortic valve implanted and subsequently the downstream flow pattern affects the grafts anastomosed to the ascending aorta, but not the internal mammary graft, which takes origin away from the downstream turbulence.

A possible limitation of our results is that the transvalvular gradient was not included in the statistical model. We believe that including the transvalvular gradient in the model would not be appropriate, since we used to measure the gradient (exposure variable) before discharge from the hospital, while the graft flow (the outcome variable) is measured intraoperatively (about 7 days earlier). Although the gradient can be measured intraoperatively by transesophageal echocardiography (transgastric alignment), the altered hemodynamics after weaning from cardiopulmonary bypass and the limitations in transducer alignment compromise the reliability and value of the intraoperative gradient. In addition, this gradient does not correlate with the postoperative probability and value of the intraoperative gradient. Nevertheless, the valve size and many other factors likely to influence the transvalvular gradient are measured intraoperatively by transesophageal echocardiography (transgastric alignment), the altered hemodynamics after weaning from cardiopulmonary bypass and the limitations in transducer alignment compromise the reliability and value of the intraoperative gradient. In addition, this gradient does not correlate with the postoperative probability and value of the intraoperative gradient. Nevertheless, the valve size and many other factors likely to influence the transvalvular gradient are included in the statistical model (Appendix A).

Another limitation of the results is that the cardiac output is not included in the model. Most of the patients had good myocardial function. Patients who got a pulmonary catheter and their cardiac outputs were measured at the time of measuring the grafts flows are too few to include the cardiac output in the statistical model. Nevertheless, the flow was measured in all patients during comparable hemodynamic conditions.

Long-term follow up of graft patency and myocardial ischemia is essential to assess the clinical relevance of our findings. We recommend that concomitant coronary artery bypass be considered a factor influencing the decision of using a biological valve in cases of aortic valve replacement. Total arterial revascularization with in-situ grafts or with the proximal anastomosis to the internal mammary artery and the use of a bileaflet valve can also be recommended if a mechanical valve to be used in a concomitant operation.

References


Appendix A

Variables studied in the initial multiple regression model for the flow in the vein grafts (missing values are 0%):

A. Patient’s data
   1. Age (71.73 ± 8.19 years)
   2. Sex (35.1% females)
   3. Body mass index (26.81 ± 4.1)
   4. Renal insufficiency (21.3%)
   5. Previous CABG (4.4%)
   6. Recent myocardial infarction (0.7%)
   7. Carotid artery stenosis (13.5%)
   8. Diabetes (31.4%)
   9. Hypertension (75.2%)

B. Cardiac data
   1. Ejection fraction (51.67 ± 16.63%)
   2. Aortic stenosis (94.3%)
   3. Aortic incompetence (50%)
   4. Atrial fibrillation (8.8%)
   5. Left main coronary artery stenosis (9.9%)
   6. Heart block (0.5%)

C. Operative data
   1. Cross clamp time (92.39 ± 24.34 min)
   2. Target coronary arteries (14.21% LAD, 12.28% diagonal, 32.41% OM, 41.1% RCA)
   3. Valve type (45.4% mechanical)
   4. Valve size (22.84 ± 2.04)
   5. Pulsatile index (2.02 ± 1.12)
   6. Hematocrit (31.08 ± 3.7%)
   7. Surgeon (seven surgeons: 22.6, 17.5, 22.6, 5.5, 18.9, 7.4 and 5.5%, respectively)